and was treated after cooling with 50 mL of water. The precipitate was filtered and recrystallized from acetonitrile to give 0.34 g (69%) of product: mp 188–190 °C; ^{1}H NMR (deuteriochloroform) δ 9.1 (m, 1 H, H-8), 7.8–6.8 (m, 9 H, H-Ar), 6.6 (s, 1 H, H-β), 3.8–2.9 (m, 8 H, H-morpholine); ^{13}C NMR (deuteriochloroform, doublet signals) δ 136.29, 134.25, 132.82, 132.76, 131.69 (2 C), 128.69, 126.87, 124.97 (2 C), 111.96, 66.72 (2C), 49.66 (2C); MS, *m/z* 427 (6%, M^+), 341 (100%, $C_{17}H_{11}BrNS^+$), 266 (5%), 260 (12%), 161 (6%), 128 (13%) (no peak at *m/z* 87). Anal. Calcd for $C_{21}H_{19}BrN_2OS$: C, 59.02; H, 4.48; N, 6.56; S, 7.50. Found: C, 58.80; H, 4.37; N, 6.38; S, 7.24.

3-(*p*-Bromophenyl)-2,3-dihydro-2-morpholinothiazolo-[2,3-*a*]isoquinolinium Fluoborate (11). To a suspension of compound **10** (0.5 g, 1.2 mmol) in 5 mL of acetonitrile was added 1 mL of 40% fluoboric acid with stirring. On addition of water, colorless crystals separated from the mixture that were recrystallized from acetonitrile–ether to give 0.43 g (71%) of product: mp 212–214 °C; ^{1}H NMR (trifluoroacetic acid) δ 9.5–7.2 (m, 10 H, H-Ar), 6.9 and 5.85 (two d, 2 H, H-2 and H-3, $J_{2,3}$ = 2.5 Hz), 3.9–2.4 (m, 8 H, H-morpholine). Anal. Calcd for $C_{21}H_{20}BBrF_4N_2OS$: C, 48.96; H, 3.91; N, 5.44; S, 6.22. Found: C, 48.74; H, 3.81; N, 5.38; S, 6.01.

2-[α-(*p*-Bromophenyl)-β-mercaptoethenyl]isoquinolin-1-(2*H*)-one (13). A mixture of thiazolium salt **9** (0.5 g, 1.2 mmol), 5 mL of acetonitrile, and 1 mL of 10% aqueous tetramethylammonium hydroxide solution was stirred for 24 h at room temperature. During this period, a colorless solution was formed first and then a slow precipitation of a white solid commenced. After filtration and recrystallization from nitromethane, 0.25 g (58%) of product was obtained: mp 210–212 °C; ^{1}H NMR (deuteriochloroform) δ 8.6 (m, 1 H, H-8), 7.9–7.1 (m, 8 H, H-Ar), 6.9 and 6.5 (two d, 2 H, H-3 and H-4, $J_{3,4}$ = 8 Hz); MS, *m/z* 357 (3%, M^+), 340 (2%), 325.0028 ($C_{17}H_{11}NOBr^+$ (M - SH)$^+$, 100). Anal. Calcd for $C_{17}H_{12}BrNOS$: C, 56.99; H, 3.38; N, 3.92; S, 8.98. Found: C, 57.01; H, 3.49; N, 3.84; S, 8.67.

α-[4-(*p*-Bromophenyl)thiazol-2-yl]-*o*-tolualdehyde (16). A mixture of thiazolium salt **6** (0.5 g, 1.2 mmol), 5 mL of acetonitrile, and 1 mL of morpholine was stirred for 1 h at room temperature, and the resulting solution was poured onto 40 g of ice water. The oily precipitate that began to crystallize slowly was filtered and was eluted on silica by ethyl acetate to give 0.26 g (62%) of product **16** mp 157–158 °C; ^{1}H NMR (deuteriochloroform) δ 10.3 (s, 1 H, H-aldehyde), 8.0–7.2 (m, 9 H, H-Ar), 4.8 (s, 2 H, CH_2). Anal. Calcd for $C_{17}H_{12}BrNOS$: C, 56.99; H, 3.38; N, 3.91; S, 8.95. Found: C, 56.85; H, 3.44; N, 3.62; S, 8.80.

Acknowledgment. Thanks are due to Dr. A. Neszmélyi for the NMR spectra and for the valuable discussions.

Registry No. **4**, 98589-68-5; **5**, 107454-06-8; **6**, 107454-08-0; **7**, 107454-02-4; **8**, 107454-03-5; **9**, 107454-04-6; **10**, 107454-05-7; **11**, 107454-11-5; **13**, 107454-09-1; **16**, 107454-12-6; *p*-bromophenacyl bromide, 99-73-0; morpholine, 110-91-8.

Supplementary Material Available: Listing of atomic coordinates and their esd values (1 page). Ordering information is given on any current masthead page.

Organoselenium-Induced Cyclization of Olefinic Imidates and Amides. Selective Synthesis of Lactams or Iminolactones

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Lactams were formed selectively by the cyclization of olefinic imidates through the addition of a phenylseleno group to the double bond. Similar cyclization of olefinic amides, on the other hand, afforded either iminolactones or lactams depending on the structure of alkenyl moiety in the amides. The structure of lactams thus produced was confirmed by their lithium aluminum hydride reduction to nitrogen heterocycles. Iminolactones bearing a chloroalkyl substituent on the imino nitrogen were utilized in the synthesis of eight- or nine-membered cyclic compounds containing both oxygen and nitrogen atoms in the ring by a novel ring-enlargement reaction.

Numerous studies have reported that the reactions of olefinic alcohols or acids with phenylselenenyl halides afford cyclic ethers[1] or lactones[2] through the addition of a phenylseleno group to the double bond and subsequent cyclization by the carbon–oxygen bond formation. These reactions have been utilized in the synthesis of natural products and related compounds.[3] Organoselenium-induced cyclization of *N*-alkenylamine derivatives has also been reported to produce pyrrolidine or piperidine derivatives[4] by the formation of a carbon–nitrogen bond. In the case of olefinic amides, we found that different type reactions proceed depending on the structure of alkenyl moiety.[5] Thus, iminolactones were produced from 4-

(1) See, for example: Nicolaou, K. C.; Magolda, R. L.; Sipio, W. J.; Barnette, W. E.; Lysenco, Z.; Joullie, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 3784–3793. Clive, D. L. J.; Chittattu, G.; Wong, C. K. *Can. J. Chem.* **1977**, *55*, 3894–3897. Clive, D. L. J.; Chittattu, G.; Curtis, N. J.; Kiel, W. A.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1977**, 725–727. Scarborough, R. M., Jr.; Smith, A. B., II; Barnette, W. E.; Nicolaou, K. C. *J. Org. Chem.* **1979**, *44*, 1742–1744. Beaulieu, P. L.; Norisset, V. M.; Garratt, D. G. *Tetrahedron Lett.* **1980**, *21*, 129–132. Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *Tetrahedron* **1985**, *41*, 5301–5306 and references cited therein.

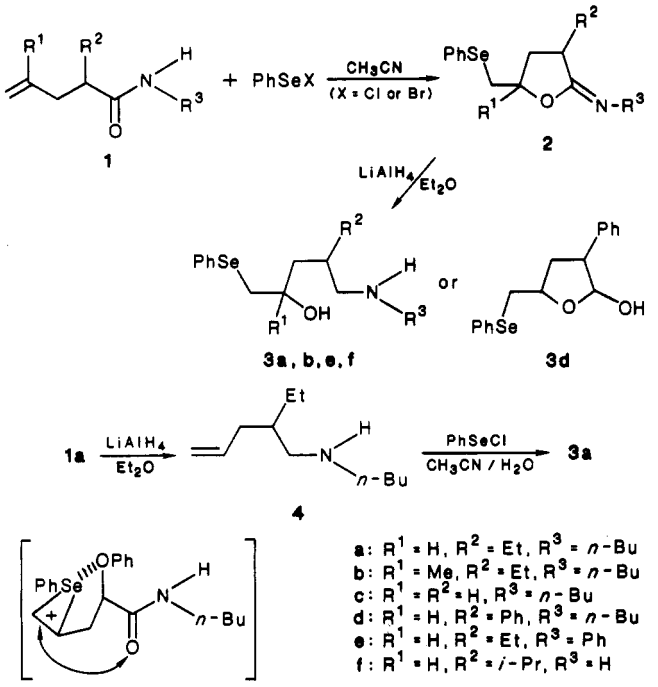
(2) See, for example: Nicolaou, K. C.; Seitz, S. P.; Sipio, W. J.; Blount, J. F. *J. Am. Chem. Soc.* **1979**, *101*, 3884–3893. Clive, D. L. J.; Russell, C. G.; Chittattu, G.; Singh, A. *Tetrahedron* **1980**, *36*, 1399–1408. Goldsmith, D.; Liotta, D.; Lee, C.; Zima, G. *Tetrahedron Lett.* **1979**, 4801–4804. Garratt, D. G.; Ryan, M. D.; Beaulieu, P. L. *J. Org. Chem.* **1980**, *45*, 839–845 and references cited therein.

(3) See, for example: Corey, E. J.; Keck, G. E.; Szekely, I. *J. Am. Chem. Soc.* **1977**, *99*, 2006–2008. Nicolaou, K. C.; Barnette, W. E.; Magolda, R. L. *Ibid.* **1981**, *103*, 3480–3485. White, J. D.; Choudhry, S. C.; Kang, M.-c. *Tetrahedron Lett.* **1984**, *25*, 3671–3674.

(4) (a) Clive, D. L. J.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Chem. Soc., Chem. Commun.* **1978**, 379–380. (b) Wilson, S. R.; Sawicki, R. S. *J. Org. Chem.* **1979**, *44*, 287–291. (c) Nicolaou, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704–3706. (d) Clive, D. L. J.; Farina, V.; Singh, A.; Wong, C. K.; Kiel, W. A.; Menchen, S. M. *J. Org. Chem.* **1980**, *45*, 2120–2126. (e) Webb, R. R., II; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 1357–1360. (f) Danishefsky, S.; Berman, E. M.; Ciufolini, M.; Etheredge, S. J.; Segmuller, B. E. *J. Am. Chem. Soc.* **1985**, *107*, 3891–3898. (g) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Org. Chem.* **1986**, *51*, 1724–1730. (h) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1837–1843.

0022-3263/87/1952-2018$01.50/0

Scheme I



pentenamide derivatives, while lactam was produced from 5-phenyl-4-pentenamide derivative. We further disclosed that the selective formation of lactams was realized by the reaction of olefinic imidates with phenylselenenyl halides through the alkyl carbon–nitrogen bond formation.[6] We describe herein the details of these new reactions.

Results and Discussion

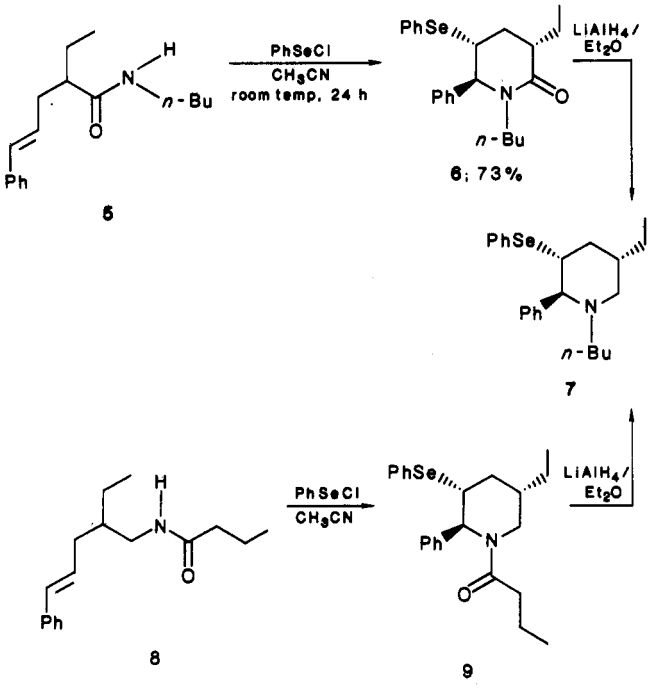
Reactions of Olefinic Amides with Phenylselenenyl Halides. By the reaction of *N*-butyl-2-ethyl-4-pentenamide (**1a**) with phenylselenenyl chloride (1 equiv) in acetonitrile as solvent at ambient temperature for 1 h, iminolactone **2a** was produced in 87% isolated yield through the attack of a carbonyl oxygen atom on an episelenonium ion intermediate (Scheme I). It was found that **2a** was unstable to silica gel and decomposed during the attempted thin-layer and column chromatography. It was necessary to use aluminum oxide chromatography for monitoring the reaction and also for the isolation of **2a**. The structure of **2a** was confirmed by lithium aluminum hydride reduction to afford amino alcohol derivative **3a**. This product was found to be identical with an authentic sample prepared by the known procedures[7] (Scheme I). *vic*-Hydroxy(phenylseleno)alkyl moiety **3a** clearly indicates that in the cyclization of **1a** selenium and oxygen atoms were introduced to the double bond of **1a**. When methyl-substituted **1b** was used as starting material, the cyclization proceeded similarly to afford iminolactone **2b** in 94% isolated yield. Although the cyclization reaction to afford iminolactones is known in the literature,[8] selenium-induced cyclizations of olefinic amides were quite scattered.[4a,9] The characteristic feature of this cyclization

Table I. Synthesis of Iminolactones[a]

starting material	X in PhSeX	time, h	product	yield,[b] %
1a	Cl	1	**2a**	87
1b	Cl	1	**2b**	94
1c	Br	2	**2c**	73
1d	Br	1	**2d**	67
1e	Br	12	**2e**	85
1f	Br	1	**2f**	80

[a] Carried out by using olefinic amide (1 mmol) and phenylselenenyl halide (1 mmol) in acetonitrile (10 mL) at ambient temperature. [b] Isolated yield by column chromatography (aluminum oxide).

Scheme II



reaction is described as follows.

The ethyl substituent on the connecting carbon chain (C_2 in **1a**) was found to be important in this cyclization reaction.[10] In the case of **1c**, which has no substituent on C_2 (R^2 = H), the expected cyclization product was not obtained by the reaction with phenylselenenyl chloride under the same condition as the reaction of **1a**. By the use of phenylselenenyl bromide, however, the cyclization of **1c** proceeded to afford the iminolactone **2c** in 73% yield. Similar to the recently reported intramolecular amidoselenation giving nitrogen heterocycles,[4g] phenylselenenyl bromide was found to be a better reagent than phenylselenenyl chloride in this intramolecular oxyselenation reaction. When an oxygen substituent was introduced into C_2 of the alkenyl group (R^2 = OPh), we could not detect the formation of cyclized product by the use of either phenylselenenyl chloride or bromide. This seems to be due to the interaction between oxygen and selenium atoms,[11] which would keep amide groups apart from an episelenonium ion as depicted in Scheme I. Although the

(5) Preliminary communication: Toshimitsu, A.; Terao, K.; Uemura, S. *Tetrahedron Lett.* **1984**, *25*, 5917–5920. It was clarified afterward that some products in this communication were erroneously assigned. The errors were corrected in the following communication.[6]

(6) Preliminary communication: Toshimitsu, A.; Terao, K.; Uemura, S. *J. Chem. Soc., Chem. Commun.* **1986**, 530–531.

(7) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Chem. Soc., Chem. Commun.* **1980**, 412–413. Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *Tetrahedron* **1985**, *41*, 5301–5306.

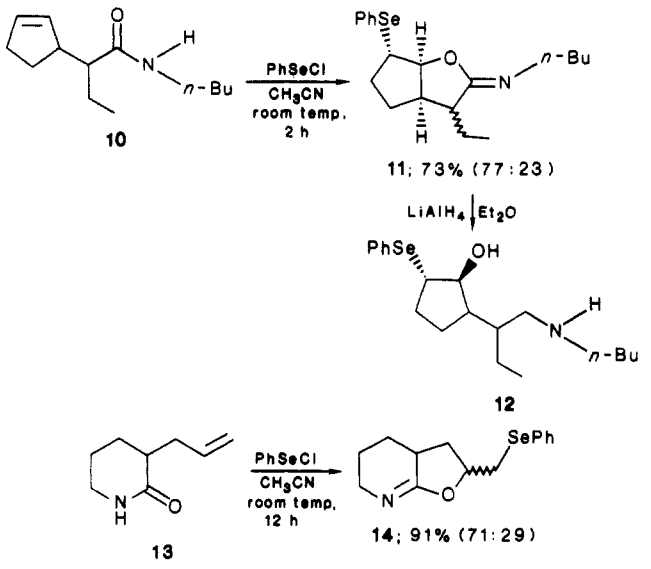
(8) Ito, Y.; Kato, H.; Saegusa, T. *J. Org. Chem.* **1982**, *47*, 741–743.

(9) Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233–3235.

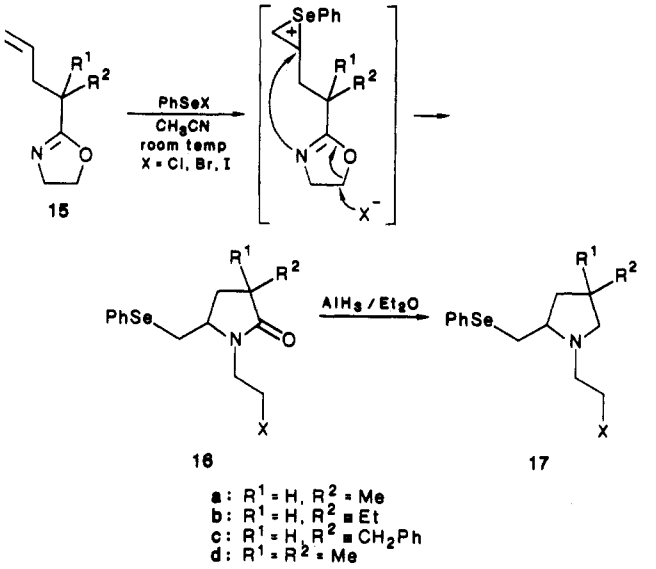
(10) As for the "buttressing effect" of the substituent, see ref 4g and references cited therein.

(11) The interaction between oxygen and selenium atoms has been postulated in the literature to explain the regio- and stereoselective addition of a phenylseleno moiety to allylic alcohol derivatives: Shimizu, M.; Takeda, R.; Kuwajima, I. *Tetrahedron Lett.* **1979**, 3461–3464. Liotta, D.; Zima, G. *J. Org. Chem.* **1980**, *45*, 2551–2553. Liotta, D.; Zima, G.; Saindane, M. *Ibid.* **1982**, *47*, 1258–1267.

Scheme III



Scheme IV



nitrogen atom is not the explicit nucleophile in this cyclization reaction, its substituent (R^3) also plays an important role. In contrast to the result of butyl-substituted **1a**, phenyl-substituted **1e** or nonsubstituted **1f** olefinic amide did not cyclize by the reaction with phenylselenenyl chloride. By the use of phenylselenenyl bromide, again, **1e** and **1f** afforded iminolactones **2e** and **2f** in excellent yields. The results are summarized in Table I. In the cases of $R^2 \neq H$, it was revealed by ^{13}C NMR that each of the iminolactones consisted of two isomers, presumably cis and trans with respect to two substituents. The nitrogen atom was lost by lithium aluminum hydride reduction of **2d** to afford lactol **3d**. The different reaction course of **2d** from that of other iminolactones may be attributed to the presence of a phenyl group on the α-carbon of the imino group.

When 5-phenylpent-4-ene derivative **5** was used as substrate, δ-lactam **6** was produced in 73% yield through carbon–nitrogen bond formation (Scheme II), in sharp contrast to the results in Scheme I. It was found by ^{13}C NMR that **6** consisted of only one stereoisomer. In the ^1H NMR spectrum of **6**, a large coupling constant between methine protons (7.8 Hz) was observed, indicating that phenylseleno and phenyl substituents are on pseudoequatorial positions. The trans relation of these substituents (erythro configuration) in **6** is a result of trans addition of phenylseleno and amide groups to the trans cinnamyl moiety. We tentatively assigned the pseudoequatorial configuration of the ethyl group considering the thermodynamical stability. The framework of **6** was confirmed by its lithium aluminum hydride reduction to piperidine derivative **7** (Scheme II). We further confirmed that **7** was identical with the authentic sample prepared by the known procedures[4g] as shown in Scheme II.[12] The reason is not yet clear why this endo cyclization (**5** → **6**) proceeded by the nitrogen atom, while exo cyclization in Scheme I proceeded by the oxygen atom.

By the reaction of phenylselenenyl chloride with an amide possessing cyclic alkene **10**, bicyclic iminolactone **11** was produced in 73% yield (Scheme III). Iminolactone **11** was found to be a mixture of two isomers which are supposed to be exo and endo with respect to the ethyl substituent. The configuration of the phenylseleno group was assigned as exo on the basis of the trans stereospecificity of the oxyselenation reactions.[13] In the case where olefinic lactam **13** was used as a starting material, a bicyclic iminolactone having endocyclic imino group **14** was produced in 91% yield. It was found that **14** was resistant to lithium aluminum hydride reduction and decomposed to unidentified compounds under forcing conditions. The ^{13}C NMR data accumulated in this study allowed the structural determination. Thus, the absorption of a carbon bound to the oxygen of iminolactones appeared at ca. 10 ppm lower field than that of a carbon bound to the nitrogen of the lactams. The carbonyl carbon of the lactams also absorbed at ca. 10 ppm lower field than the imine carbon of iminolactones. In addition to these criteria, IR as well as ^1H NMR spectra provided supports for the structural determination. In ^1H NMR, the proton geminal to the oxygen of iminolactones absorbed at ca. 4.5 ppm, while the proton geminal to the nitrogen of lactams absorbed at a higher field than 4.0 ppm. In IR spectra, the carbonyl absorption of lactams was found around 1690 cm^{-1}, and the imine absorption of iminolactones was observed about 1705 cm^{-1}. In all these respects, the cyclization products from **13** were assigned as **14**.

Table II. Cyclization of 15 to γ-Lactams[a]

starting material	X in PhSeX and product	time, h	product	yield,[b] %
15a	Cl	12	**16a**	60
15a	Br	12	**16a**	58
15b	Cl	2	**16b**	67
15c	Cl	12	**16c**	62
15c	Br	36	**16c**	61
15d	Cl	2	**16d**	93
15d	Cl	12	**16d**	100
15d	Br	2	**16d**	81
15d	I	2	**16d**	61

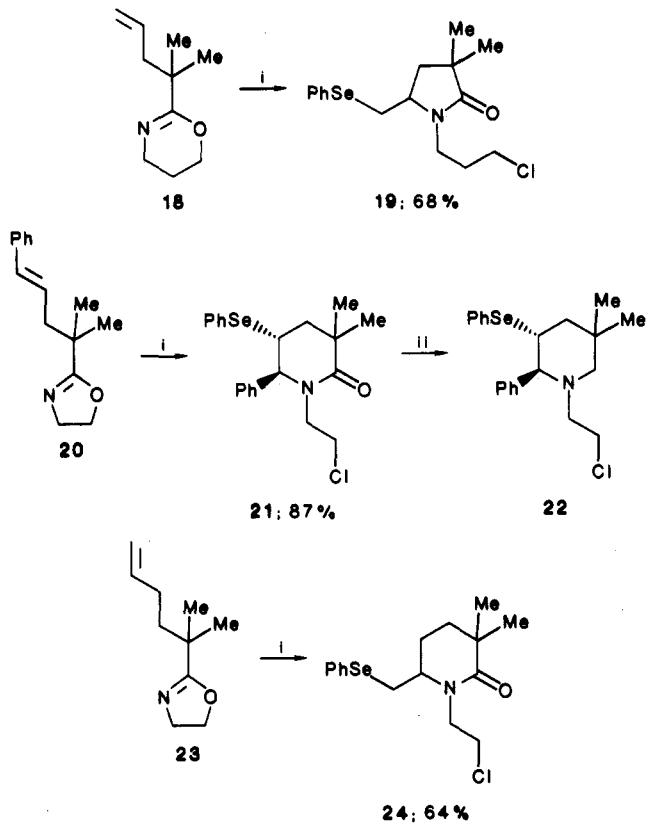
[a] Carried out by using olefinic oxazoline (1 mmol) and phenylselenenyl chloride (1 mmol) in acetonitrile (10 mL) at ambient temperature. [b] Isolated yield by column chromatography (silica gel).

Reactions of Olefinic Imidates with Phenylselenenyl Halides. By the reaction of an olefinic imidate

(12) Although it was ascertained by ^{13}C NMR that **9** consisted of one stereoisomer, lithium aluminum hydride reduction products from **9** were found to be a mixture of isomers, namely, **7** and its isomer. The three substituents on the ring carbon atoms should be intact during the reduction, and the isomer seems to be the one as for the substituent on the nitrogen atom. The details are, however, not yet known.

(13) See, for example: Toshimitsu, A.; Aoai, T.; Uemura, S.; Okano, M. *J. Org. Chem.* **1980**, *45*, 1953–1958.

Scheme V[a]



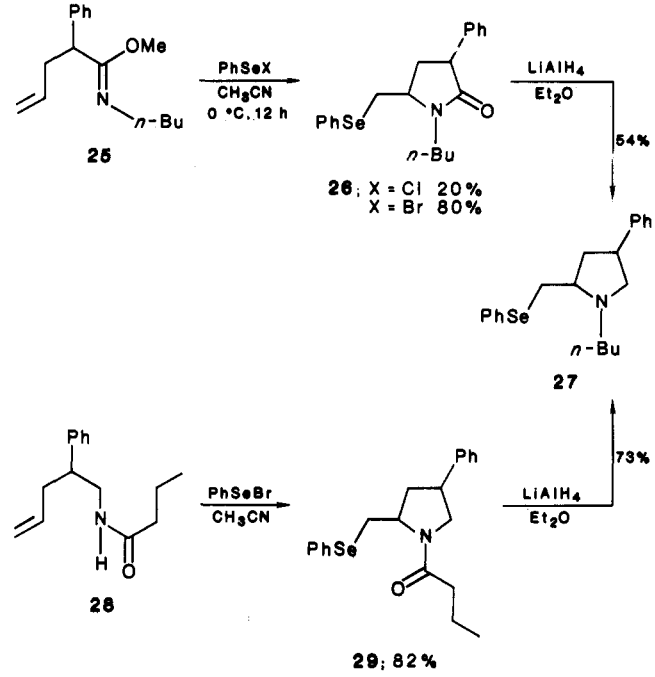
[a] Reagent: (i) PhSeCl in CH_3CN, 20 °C, 24–48 h; (ii) AlH_3 in Et_2O.

such as 2-(3-butenyl)oxazoline derivatives **15a** with phenylselenenyl halide, γ-lactam **16a** was produced through the attack of a nitrogen atom on an episelenonium ion and the ring opening of the oxazoline by a halide anion (Scheme IV). γ-Lactams thus produced were found to be stable to silica gel thin-layer as well as column chromatography, in sharp contrast to **2** in Scheme I. Neither cyclization by oxygen atom nor formation of δ-lactam was observed in the selenium-induced cyclization of **15**. As summarized in Table II, the effect of substituent at the connecting carbon chain is also remarkable in this cyclization reaction, and the yield of dimethyl-substituted **16d** was much better than those of monosubstituted **16a–c**. The structure of **16** was confirmed by metal hydride reduction of the carbonyl group to afford pyrrolidine derivatives **17**, phenylseleno and haloethyl substituents remaining intact. When lithium aluminum hydride was used, the yield of **17d** (X = Br) was unsatisfactory (29%). With aluminum hydride,[14] the yields of **17** were much improved in both cases X = Br and X = Cl [**17d** (X = Br), 80%; **17c** (X = Cl), 88%; **17d** (X = Cl), 79%].

Ring opening of the six-membered cyclic imidate **18** also proceeded with phenylselenenyl chloride to afford γ-lactam **19** having a chloropropyl substituent on nitrogen atom. When an oxazoline having 4-phenylbut-3-enyl substituent **20** was used as a starting material, endo cyclization occurred to give the δ-lactam **21**. It was confirmed by ^{13}C and ^1H NMR that **21** consisted of one stereoisomer, as in the case of **6** (Scheme II). From 2-(4-pentenyl)oxazoline derivative **23**, δ-lactam having (phenylseleno)methyl substituent (**24**) was produced through exo cyclization as in the cases of **15** and **18**. The results are summarized in Scheme V.

(14) Nystrom, R. F. *J. Am. Chem. Soc.* **1955**, *77*, 2544–2545.

Scheme VI



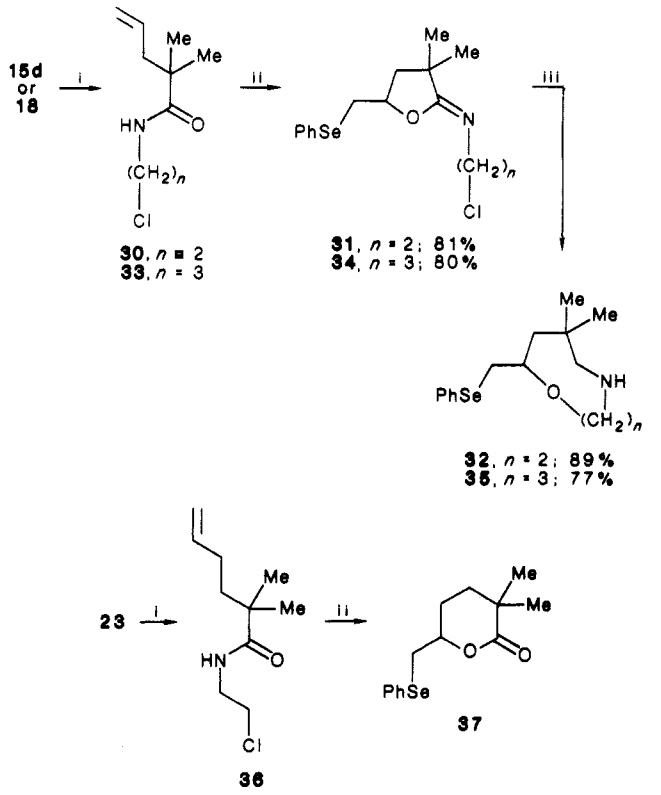
We also examined the reactions of acyclic olefinic imidates with phenylselenenyl halides. The reaction of methyl *N*-butyl-2-phenylpent-4-enimidate (**25**) with phenylselenenyl bromide led to γ-lactam **26** through exo cyclization by the formation of a carbon–nitrogen bond (Scheme VI). This reaction was carried out at a concentration of 1.0×10^{-2} M of the substrate at 0 °C because the yields of **26** were inferior at higher temperatures or concentrations due to side reactions. Another characteristic feature in the linear case is the effect of the gegen anion of the selenenylating reagent. In contrast to the case of the cyclic imidate, phenylselenenyl chloride gave lactam **26** in much lower yield than in the case of phenylselenenyl bromide. The structure of **26** was also confirmed by its lithium aluminum hydride reduction to a pyrrolidine derivative (**27**).

These results clearly indicate the difference in reactivity between an amide and an imidate. The amide can react at either oxygen or nitrogen in the intramolecular reaction with an episelenonium ion, and the structure of the substrate determines the course of the cyclization (Schemes I–III). On the other hand, the imidate reacts exclusively at nitrogen with an episelenonium ion intramolecularly to afford the lactams (Schemes IV–VI).

Ring Enlargement of *N*-Haloalkyl Iminolactones to Medium-Sized Heterocycles. Olefinic imidates **15d**, **18**, and **23** were converted to the corresponding olefinic amides, **30**, **33**, and **36**, respectively, with anhydrous HCl.[15] By the reaction of **30** and **33** with phenylselenenyl bromide, iminolactones **31** and **34** were produced in excellent yields (Scheme VII). In order to confirm its structure, **31** was subjected to lithium aluminum hydride reduction. Unexpectedly, the product was found to be an eight-membered cyclic compound (**32**) containing both oxygen and nitrogen atoms in the ring (Scheme VII). Mass spectrum of **32** shows the absence of chlorine atom, and its ^{13}C NMR spectrum supports the cyclic structure (see the Experimental Section). This ring-enlargement reaction apparently includes a nucleophilic substitution of chlorine

(15) Saito, S.; Tamai, H.; Usui, Y.; Inaba, M.; Moriwake, T. *Chem. Lett.* **1984**, 1243–1246.

Scheme VII[a]

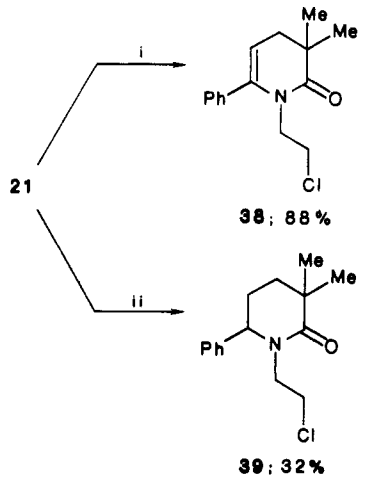


[a] Reagent: (i) $Me_3SiCl/MeOH$; (ii) $PhSeBr/CH_3CN$, 20 °C; (iii) $LiAlH_4/Et_2O$.

by oxygen and a bond fission between oxygen and an imino carbon atom, but the details are not yet clear. Nine-membered cyclic compound **35** was also produced by the extension of the chloroalkyl carbon chain (**34**). This novel ring-enlargement reaction is useful, as medium-sized cyclic compounds such as **32** and **35** are difficult to access by other procedures. Another approach to a nine-membered cyclic compound did not succeed as the selenium-induced cyclization product from **36** was found to be δ-lactone **37**. This lactone formation may be explained as follows: cyclization by an oxygen atom proceeded to afford a six-membered iminolactone which was less stable than other iminolactones and hydrolyzed to **37** during a similar isolation procedure.

Oxidative and Reductive Removal of the Phenylseleno Group from Lactam 21. The results of oxidative and reductive removal of a phenylseleno group from δ-lactam **21** thus prepared are described briefly. In our previous study of *N*-acetylpiperidine derivatives,[4g] we reported that the amide group is less effective than the phenyl group in determining the direction of the selenoxide elimination; i.e., selectivity of selenoxide elimination "away" from the amide group[16] was altered by conjugation with the phenyl group to give the vinylic amide derivative. As **21** is a good candidate to test the generality of our previous observation,[4g] we investigated the oxidative elimination of **21**. The product was found to be vinylic amide **38** in which a double bond was conjugated with the phenyl group (Scheme VIII). It was confirmed that our previous observation also stands in this δ-lactam system. The selective removal of a phenylseleno group from **21** was tried by nickel boride reduction[17] and **39** was obtained in

Scheme VIII[a]



[a] Reagent: (i) O_3 in CH_2Cl_2 at −78 °C, then Et_3N in CCl_4 at reflux; (ii) $NiCl_2·6H_2O$, $NaBH_4$ in THF–MeOH.

32% yield, the carbonyl group and a chlorine substituent remaining intact.

Experimental Section

IR spectra were recorded with a JASCO IR-810 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with JEOL JNM-FX-100 (100 MHz) and JEOL JNM-GX-400 (400 MHz) instruments on solutions in $CDCl_3$ with Me_4Si as an internal standard. Melting points were determined with a Shimadzu MM-2 micro melting point determination apparatus and were uncorrected. Mass spectra were measured on a JEOL JMS DX 300 mass spectrometer.

Phenylselenenyl bromide and iodide were prepared by a reported procedure.[4g] Tetrahydrofuran (THF) and diethyl ether were dried over benzophenone ketyl and were distilled just before use. A solution of *n*-butyllithium in hexane (1.5 M) and *N*-trimethylsilylacetamide were commercial products and were used without purification. *N*-Butylbutanamide was prepared by the reaction of butanoyl chloride with butylamine in the presence of triethylamine. All other organic materials were commercial products and were purified before use by distillation. Aluminum trichloride was purified before use by sublimation. All other inorganic materials were commercial products and were used without purification.

Preparation of *N*-Butyl-2-ethylpent-4-enamide (1a). General Procedure. To a solution of *N*-butylbutanamide (2.86 g, 20 mmol) in THF (45 mL) was added a solution of *n*-butyllithium in hexane (26.7 mL, 40 mmol) at ambient temperature under nitrogen atmosphere, and the resulting solution was stirred at the same temperature for 0.5 h. Then allyl bromide (1.73 mL, 20 mmol) was added, and the resulting solution was stirred at ambient temperature for 1 h. The reaction was quenched by the addition of distilled water (30 mL), and the products were extracted with dichloromethane (40 mL × 5). The organic layer was dried ($MgSO_4$) and evaporated to leave a yellow oil. Column chromatography of this oil (silica gel, hexane–ethyl acetate (10:1) as eluant) afforded **1a** (2.05 g, 10 mmol, 50%): IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 0.90 (t, 3 H, J = 7.3 Hz), 0.92 (t, 3 H, J = 7.3 Hz), 1.1–1.8 (m, 6 H), 1.8–2.4 (m, 3 H), 3.26 (q, 2 H, J = 6.4 Hz), 5.00 (br d, 1 H, J = 9.8 Hz), 5.04 (br d, 1 H, J = 17.9 Hz), 5.76 (ddt, 1 H, J = 17.9, 9.8, and 6.8 Hz), and 5.5–5.9 (br s, 1 H); high-resolution mass spectrum, M^+ calcd for $C_{11}H_{21}NO$ 183.1623, found 183.1635.

Preparation of 2-Isopropylpent-4-enamide (1f). To a solution of *N*-trimethylsilylacetamide (4.0 g, 30.6 mmol) in THF (80 mL) was added a solution of *n*-butyllithium in hexane (40.8 mL, 61.2 mmol) under ice-bath cooling in nitrogen atmosphere.

(16) (a) Toshimitsu, A.; Aoai, T.; Owada, H.; Uemura, S.; Okano, M. *J. Org. Chem.* **1981**, *46*, 4727–4733. (b) Uemura, S.; Toshimitsu, A. *Bull. Inst. Chem. Res., Kyoto Univ.* **1984**, *62*, 105–123.

(17) Back, T. G. *J. Chem. Soc., Chem. Commun.* **1984**, 1417–1418. See also: Barton, D. H. R.; Britten-Kelly, M. R.; Ferreira, D. J. *Chem. Soc., Perkin Trans. 1* **1978**, 1090–1110. Barton, D. H. R.; Lusinchi, X.; Milliet, P. *Tetrahedron Lett.* **1982**, *23*, 4949–4952.

After 0.5 h, allyl bromide (2.64 mL, 30.6 mmol) was added, and the resulting solution was stirred at the same temperature for 2 h. Then *n*-butyllithium in hexane (20.4 mL, 30.6 mmol) and isopropyl iodide (3.06 mL, 30.6 mmol) were added by the same procedure. After the workup as described above, the organic layer was washed by 5% aqueous HCl (50 mL) and brine (20 mL) successively and then dried ($MgSO_4$) and evaporated. Column chromatography (silica gel, hexane–ethyl acetate (2:1) as eluant) of the residual oil afforded **1f** (1.46 g, 10.4 mmol, 34%): mp 98–100 °C; IR (KBr disk) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 0.98 (d, 6 H, J = 5.9 Hz), 1.7–2.05 (m, 2 H), 2.2–2.4 (m, 2 H), 5.03 (br d, 1 H, J = 10.3 Hz), 5.08 (br d, 1 H, J = 17.1 Hz), 5.3–5.7 (br s, 2 H), 5.80 (ddt, 1 H, J = 17.1, 10.3 and 6.8 Hz); high-resolution mass spectrum, M^+ calcd for $C_8H_{15}NO$ 141.1153, found 141.1140.

Reaction of 1a with Phenylselenenyl Chloride. General Procedure for Intramolecular Oxyselenation Reaction. To a solution of **1a** (0.213 g, 1.0 mmol) in acetonitrile (3 mL) was added a solution of phenylselenenyl chloride (0.197 g, 1.0 mmol) in the same solvent (7 mL) at ambient temperature, and the resulting yellow solution was stirred for 1 h. After the addition of saturated aqueous $NaHCO_3$ (20 mL), the products were extracted with dichloromethane (20 mL × 4). The organic layer was washed with brine, dried, and evaporated to leave a yellow oil. Column chromatography (aluminum oxide, Woelm B (type W 200) activity grade V, hexane–ethyl acetate (20:1) as eluant) of this oil afforded *N*-butyl-2-ethyl-4-[(phenylseleno)methyl]imino-γ-butyrolactone (**2a**) as a pale yellow oil (0.284 g, 0.87 mmol, 87%) (a mixture of two isomers; ca. 65:35): IR (film) 1703 cm^{-1}; ^1H NMR (100 MHz) δ 0.8–1.0 (m, 6 H), 1.1–1.7 (m, 5 H), 1.7–2.2 (m, 2 H), 2.3–2.8 (m, 2 H), 2.8–3.4 (m, 4 H), 4.3–4.7 (m, 1 H), 7.2–7.3 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ major isomer 11.6 (q), 14.0 (q), 20.7 (t), 25.0 (t), 25.9 (t), 32.5 (t), 33.1 (t), 42.6 (d), 46.8 (t), 78.5 (d), 163.2 (s), and phenyl signals; minor isomer 11.6 (q), 14.0 (q), 20.7 (t), 23.3 (t), 25.0 (t), 34.0 (t), 35.7 (t), 41.5 (d), 46.8 (t), 78.8 (d), 164.0 (s), and phenyl signals; mass spectrum, M^+ 339, 337.

To a suspension of lithium aluminum hydride (LAH) (0.057 g, 1.5 mmol) in diethyl ether (2 mL) was added a solution of **2a** (0.246 g, 0.7 mmol) in the same solvent (1 mL) at 0 °C, and the resulting mixture was stirred at 0 °C for 0.5 h and then at ambient temperature for 11 h. The usual workup[4g] (silica gel, ethyl acetate as eluant) afforded butyl[2-ethyl-4-hydroxy-5-(phenylseleno)-pentyl]amine (**3a**) (0.175 g, 0.51 mmol, 73%) (a mixture of two isomers; ca. 55:45): IR (film) 3275, 2965, 2933, 2878, 1480, 738, and 695 cm^{-1}; ^1H NMR (100 MHz) δ 0.90 (t, 6 H, J = 6.8 Hz), 1.1–1.6 (m, 7 H), 1.65–2.05 (m, 2 H), 2.2–2.75 (m, 5 H), 2.8–3.3 (m, 3 H), 3.6–4.0 (m, 1 H), 7.1–7.3 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ (*two signals overlapping) major isomer 11.8 (q), 13.9 (q), 20.4 (t), 25.6 (t), 31.7 (t), 36.3 (t), 40.9 (d), 43.9 (t), 49.4 (t), 53.6 (t), 66.9 (d), 126.4 (d), 128.9 (d)*, 131.2 (s), 132.2 (d)*; minor isomer 11.4 (q), 13.9 (q), 20.4 (t), 28.5 (t), 31.7 (t), 35.3 (t), 36.9 (d), 40.4 (t), 49.6 (t), 55.5 (t), 71.0 (d), 126.4 (d), 128.9 (d)*, 130.9 (s), 132.2 (d)*. Anal. Calcd for $C_{17}H_{29}NOSe$: C, 59.64; H, 8.54; N, 4.09. Found: C, 59.35; H, 8.38; N, 4.17.

An authentic sample of **3a** was prepared as follows. The LAH reduction of **1a** (in Et_2O, reflux, 12 h) afforded butyl(2-ethylpent-4-enyl)amine (**4**) in 38% yield: IR (film) 2957, 2923, 2870, 2853, 1458, and 905 cm^{-1}; ^1H NMR (100 MHz) δ 0.89 (t, 3 H, J = 6.6 Hz), 0.91 (t, 3 H, J = 7.3 Hz), 1.05–1.7 (m, 8 H), 2.08 (dd, 2 H, J = 6.8 and 6.3 Hz), 2.4–2.7 (m, 4 H), 4.99 (br d, 1 H, J = 9.3 Hz), 5.01 (br d, 1 H, J = 15.1 Hz), 5.76 (ddt, 1 H, J = 9.3, 15.1, and 6.8 Hz). Hydroxyselenation of **4** was carried out by a reported procedure[7] by the reaction with phenylselenenyl chloride in acetonitrile–water (5:1) to give the adducts in 85% yield. The adducts consisted of only the Markovnikov type addition products (as a mixture of diastereoisomers). ^{13}C NMR spectrum of **3a** was confirmed to be identical with that of this sample.

2-Isopropyl-4-[(phenylseleno)methyl]imino-γ-butyrolactone (2f) (a mixture of two isomers; ca. 57:43): IR (film) 1705 cm^{-1}; ^1H NMR (100 MHz) δ 0.89 (t, 3 H, J = 6.8 Hz), 0.99 (t, 3 H, J = 6.8 Hz, minor isomer), 1.01 (t, 3 H, J = 6.8 Hz, major isomer), 1.4–1.9 (m, 1 H), 1.9–2.4 (m, 2 H), 2.55–2.8 (m, 1 H), 2.8–3.35 (m, 2 H), 4.2–4.6 (m, 1 H), 6.3–7.4 (br s, 1 H), 7.2–7.3 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ major isomer 17.0 (q), 21.2 (q), 27.7 (d), 30.8 (t), 31.9 (t), 46.8 (d), 78.0 (d), 127.2 (d), 129.1 (d)*, 129.1 (s), 132.9 (d)*, and 173.1 (s); minor isomer 17.7 (q), 20.7 (q), 29.4 (d), 30.2 (t), 32.4 (t), 45.6 (d), 78.8 (d), 127.2 (d), 129.1 (d)*, 129.1 (s), 132.9 (d)*, and 173.8 (s). Anal. Calcd for $C_{14}H_{19}NOSe$: C, 56.75; H, 6.46; N, 4.73. Found: C, 56.70; H, 6.40; N, 4.61.

2-Isopropyl-4-hydroxy-5-(phenylseleno)pentylamine (3f) (a mixture of two isomers; ca. 53:47): IR (film) 3360, 3285, 3050, 2950, 2924, 2868, 1475, 1020, 736, and 688 cm^{-1}; ^1H NMR (100 MHz) δ 0.8–1.0 (m, 6 H), 1.2–2.0 (m, 4 H), 2.3–3.2 (m, 4 H), 3.2–3.6 (br s, 3 H), 3.6–4.1 (m, 1 H), 7.1–7.3 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ major isomer 19.5 (q), 20.0 (q), 29.5 (d), 36.5 (t), 37.8 (t), 45.0 (t), 46.7 (d), 71.3 (d), 126.4 (d), 128.9 (d)*, 130.9 (s), and 132.1 (d)*; minor isomer 18.6 (q), 19.5 (q), 32.4 (d), 35.5 (t), 40.2 (t), 42.5 (d), 43.6 (t), 67.3 (d), 126.5 (d), 128.9 (d)*, 131.2 (s), 132.1 (d)*. Anal. Calcd for $C_{14}H_{23}NOSe$: C, 56.00; H, 7.72; N, 4.66. Found: C, 56.12; H, 7.62; N, 4.59.

Reaction of 5 with Phenylselenenyl Chloride. To a solution of **5** (0.259 g, 1.0 mmol) in acetonitrile (5 mL) was added a solution of phenylselenenyl chloride (0.197 g, 1.0 mmol) in the same solvent (5 mL), and the resulting solution was stirred at ambient temperature for 24 h. After the workup as described above, column chromatography [silica gel, hexane–ethyl acetate (5:1) as eluant] afforded *N*-butyl-2-ethyl-4-(phenylseleno)-5-phenyl-δ-valerolactam (**6**) (0.310 g, 0.73 mmol, 73%): IR (film) 1645 cm^{-1}; ^1H NMR (100 MHz) δ 0.81 (t, 3 H, J = 6.8 Hz), 0.93 (t, 3 H, J = 7.3 Hz), 1.1–1.5 (m, 4 H), 1.5–1.8 (m, 1 H), 1.8–2.1 (m, 2 H), 2.1–2.6 (m, 3 H), 3.42 (ddd, 1 H, J = 10.3, 7.8, and 3.9 Hz), 3.83 (dt, 1 H, J = 13.7 and 7.3 Hz), 4.49 (d, 1 H, J = 7.8 Hz), and 7.1–7.45 (m, 10 H); ^{13}C NMR (25 MHz) δ 11.5 (q), 13.7 (q), 20.0 (t), 24.7 (t), 29.1 (t), 32.3 (t), 43.1 (d), 44.6 (t), 45.0 (d), 66.9 (d), 172.2 (s), and phenyl signals. Anal. Calcd for $C_{23}H_{29}NOSe$: C, 66.66; H, 7.05; N, 3.38. Found: C, 66.36; H, 7.11; N, 3.30.

The reduction of **6** was carried out by using **6** (0.330 g, 0.8 mmol) and LAH (0.061 g, 1.6 mmol) in diethyl ether (8 mL) at 0 °C for 15 min to afford *N*-butyl-5-ethyl-2-phenyl-3-(phenylseleno)-piperidine (**7**) (0.179 g, 0.45 mmol, 56%): IR (film) 2960, 1455, 740, 700, and 695 cm^{-1}; ^1H NMR (400 MHz) δ 0.72 (t, 3 H, J = 7.3 Hz), 0.87 (t, 3 H, J = 7.3 Hz), 0.9–1.3 (m, 2 H), 1.3–1.6 (m, 4 H), 1.6–1.7 (m, 2 H), 1.80 (t, 1 H, J = 11.0 Hz), 1.94 (ddd, 1 H, J = 13.2, 6.8, and 6.4 Hz), 2.19 (br d, 1 H, J = 14.7 Hz), 2.35 (ddd, 1 H, J = 13.2, 8.3, and 7.3 Hz), 3.09 (d, 1 H, J = 10.3 Hz), 3.10 (br d, 1 H, J = 10.3 Hz), 3.35 (ddd, 1 H, J = 12.2, 10.3, and 3.9 Hz), 7.05–7.35 (m, 10 H); ^{13}C NMR (25 MHz) δ 11.3 (q), 13.9 (q), 20.4 (t), 27.1 (t), 27.7 (t), 39.0 (d), 40.5 (t), 49.4 (d), 54.8 (t), 58.4 (t), 73.6 (d), and phenyl signals; mass spectrum, M^+: 401, 399. Anal. Calcd for $C_{23}H_{31}NSe$: C, 68.98; H, 7.80; N, 3.50. Found: C, 68.95; H, 7.70; N, 3.47.

An authentic sample of **7** was prepared as follows. *N*-(2-Ethyl-5-phenylpent-4-enyl)butanamide (**8**) was prepared from butyronitrile:[4g] IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 0.93 (t, 3 H, J = 7.3 Hz), 0.95 (t, 3 H, J = 6.6 Hz), 1.2–1.8 (m, 5 H), 2.05–2.3 (m, 4 H), 3.26 (dd, 1 H, J = 6.4 and 5.9 Hz), 3.27 (dd, 1 H, J = 6.4 and 5.9 Hz), 5.4–5.6 (br s, 1 H), 6.26 (dt, 1 H, J = 15.6 and 6.4 Hz), 6.36 (d, 1 H, J = 15.6 Hz), and 7.15–7.35 (m, 5 H); mass spectrum, M^+ 259.

The cyclization of **8** (0.519 g, 2.0 mmol) was carried out by the reaction with phenylselenenyl chloride (0.395 g, 2.0 mmol) in acetonitrile (20 mL) (room temperature, 18 h) to afford *N*-butanoyl-5-ethyl-2-phenyl-3-(phenylseleno)piperidine (**9**) (0.556 g, 1.3 mmol, 65%): IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 0.88 (t, 3 H, J = 7.3 Hz), 0.90 (t, 3 H, J = 6.6 Hz), 1.3–2.05 (m, 7 H), 2.05–2.6 (m, 4 H), 3.6–4.0 (m, 1 H), 5.2–5.3 (m, 1 H), 7.0–7.4 (m, 8 H), and 7.45–7.75 (m, 2 H); ^{13}C NMR (25 MHz) δ 10.9 (q), 13.9 (q), 18.5 (t), 27.4 (t), 32.2 (t), 32.6 (t) 34.9 (t), 35.3 (d), 43.4 (d), 59.8 (d), 173.3 (s), and phenyl signals; mass spectrum, M^+ 415, 413.

The reduction of **9** (0.207 g, 0.5 mmol) was carried out by using LAH (0.038 g, 1.0 mmol) in diethyl ether (3 mL) at 0 °C for 0.5 h and then at ambient temperature for 2 h to afford **7** as a mixture of isomers, which were separable by preparative TLC [Merck, silica gel 60 F_{254} PLC plate (20 cm × 20 cm × 2 mm), hexane–ethyl acetate (5:1) as eluant]. Isomer of higher R_f value (0.100 g, 0.25 mmol, 50%): IR (film) 2960, 1455, 740, 700, and 690 cm^{-1}; ^1H NMR (400 MHz) δ 0.72 (t, 3 H, J = 7.3 Hz), 0.88 (t, 3 H, J = 7.3 Hz), 0.9–1.1 (m, 1 H), 1.15–1.3 (m, 2 H), 1.3–1.4 (m, 1 H), 1.5–1.6 (m, 1 H), 1.6–1.65 (m, 1 H), 1.7–1.8 (m, 2 H), 1.87 (ddd, 1 H, J = 12.2, 8.3, and 3.9 Hz), 2.03 (d, quint, 1 H, J = 13.7 and 2.2 Hz),

2.22 (dd, 1 H, J = 11.2 and 3.4 Hz), 2.30 (dt, 1 H, J = 12.2 and 7.8 Hz), 2.99 (dt, 1 H, J = 9.8 and 2.2 Hz), 3.15 (d, 1 H, J = 9.8 Hz), 3.49 (ddd, 1 H, J = 12.2, 9.8, and 3.9 Hz), and 7.1–7.35 (m, 10 H); ^{13}C NMR (25 MHz) δ 12.2 (q), 13.9 (q), 20.1 (t), 23.9 (t), 28.6 (t), 36.9 (d), 37.5 (t), 46.5 (d), 54.3 (t), 55.0 (t), 74.0 (d), and phenyl signals; mass spectrum, M^+ 401, 399. Anal. Calcd for $C_{23}H_{31}NSe$: C, 68.98; H, 7.80; N, 3.50. Found: C, 69.04; H, 7.69; N, 3.48. Isomer of lower R_f value (reduction product from **6** was identical with this sample) (0.075 g, 0.2 mmol, 40%).

8-[(Phenylseleno)methyl]-9-oxa-2-azabicyclo[4.3.0]non-1-ene (14) (a mixture of two isomers; ca. 71:29): IR (film) 1703 cm^{-1}; ^{1}H NMR (100 MHz) δ 1.15–1.95 (m, 4 H), 2.0–2.6 (m, 3 H), 2.88 (dd, 1 H, J = 12.7 and 9.3 Hz, minor isomer), 2.95 (dd, 1 H, J = 12.7 and 8.3 Hz, major isomer), 3.1–3.6 (m, 3 H), 4.1–4.6 (m, 1 H), 7.2–7.4 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25.1 MHz) δ major isomer 21.8 (t), 25.6 (t), 31.7 (t), 36.3 (d), 37.2 (t), 46.7 (t), 77.5 (d), 168.5 (s), and phenyl signals; minor isomer 21.8 (t), 25.6 (t), 31.2 (t), 32.5 (d), 33.7 (t), 46.7 (t), 76.6 (d), 168.8 (s), and phenyl signals. Anal. Calcd for $C_{14}H_{17}NOSe$: C, 57.15; H, 5.82; N, 4.76. Found: C, 57.09; H, 5.84; N, 4.69.

Preparation of 2-(1,1-Dimethylbut-3-enyl)oxazoline (15d). General Procedure. To a solution of lithium diisopropylamide (LDA) (0.08 mol) in THF (80 mL) and hexane (54 mL) was added a solution of 2-ethyloxazoline (8.1 mL, 0.08 mol) in THF (10 mL) at −78 °C under nitrogen atmosphere, and the solution was stirred at −60 °C for 2 h. Then methyl iodide (5.0 mL, 0.08 mol) was added at −78 °C, and the resulting solution was stirred at −55 °C for 2 h. The reaction was quenched by the addition of 10% aqueous NH_4Cl (80 mL), and the products were extracted with diethyl ether (50 mL × 4). Distillation of the dried ($MgSO_4$) organic layer (70 °C (25 mmHg)) afforded 2-isopropyloxazoline (6.5 g, 0.057 mol, 71%).

To a solution of LDA (0.042 mol) in THF (45 mL) and hexane (28 mL) was added a solution of 2-isopropyloxazoline (4.5 g, 0.04 mol) in THF (10 mL) at −78 °C under nitrogen atmosphere, and the solution was stirred at −60 °C for 1.5 h. Then allyl bromide (3.6 mL, 0.042 mol) was added at −70 °C, and the resulting solution was stirred at −50 °C for 2 h.

After the workup as described above, **15d** (4.34 g, 28 mmol, 71%) was isolated by distillation (75–83 °C (23 mmHg)): IR (film) 1655 cm^{-1}; ^{1}H NMR (100 MHz) δ 1.20 (s, 6 H), 2.28 (br d, 2 H, J = 7.3 Hz), 3.81 (t, 1 H, J = 8.8 Hz), 3.85 (dd, 1 H, J = 10.3 and 9.3 Hz), 4.17 (dd, 1 H, J = 9.3 and 8.8 Hz), 4.18 (dd, 1 H, J = 10.3 and 8.8 Hz), 4.9–5.1 (m, 2 H), 5.77 (ddt, 1 H, J = 17.6, 9.3, and 7.3 Hz). Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87, N, 9.14. Found: C, 70.49; H, 9.83; N, 8.86.

2-(1,1-Dimethylbut-3-enyl)-5,6-dihydro-4*H*-1,3-oxazine (18). 2-Methyl-5,6-dihydro-4*H*-1,3-oxazine was prepared by the modified method[18] of the reported procedure[19] in which (1) 3-aminopropanol was added to the mixture of acetonitrile and cadmium(II) acetate over 3 h, maintaining the bath temperature at 100 °C, and (2) the resulting mixture was stirred under heating in the same bath for 24 h. 2-Methyl-5,6-dihydro-4*H*-1,3-oxazine, thus prepared, was allylated (bp 100 °C (50 mmHg)) and methylated (bp 110 °C (40 mmHg)) successively in the same procedure as described above. The final lithiation was carried out in the presence of 2 equiv of hexamethylphosphoric triamide (HMPA) and methylated as described above to afford **18**, which was purified by column chromatography (aluminum oxide Woelm B (type W 200) activity grade V, hexane as eluant) and then by distillation (bp 110 °C (30 mmHg)): IR (film) 1667 cm^{-1}; ^{1}H NMR (100 MHz) δ 1.09 (s, 6 H), 1.81 (tt, 2 H, J = 5.9 and 5.4 Hz), 2.21 (d, 2 H, J = 7.3 Hz), 3.38 (t, 2 H, J = 5.9 Hz), 4.13 (t, 2 H, J = 5.4 Hz), 4.9–5.1 (m, 2 H), 5.77 (ddt, 1 H, J = 17.6, 10.3, and 7.3 Hz). Anal. Calcd for $C_{10}H_{17}NO$: C, 71.81; H, 10.24; N, 8.37. Found: C, 71.45; H, 10.31; N, 8.47.

Reaction of 15d with Phenylselenenyl Chloride. General Procedure for Intramolecular Amidoselenation of Cyclic Alkenyl Imidates. To a solution of **15d** (0.306 g, 2.0 mmol) in acetonitrile (10 mL) was added a solution of phenylselenenyl chloride (0.395 g, 2.0 mmol) in the same solvent (10 mL), and the resulting colorless solution was stirred at ambient temperature for 24 h. The solvents were removed under reduced pressure, and column chromatography [silica gel, hexane–ethyl acetate (5:1) as eluant] of the residual oil afforded *N*-(2-chloroethyl)-2,2-dimethyl-4-[(phenylseleno)methyl]-γ-butyrolactam (**16d**; X = Cl) (0.710 g, 2.0 mmol, 100%): IR (film) 1685 cm^{-1}; ^{1}H NMR (100 MHz) δ 1.13 (s, 3 H), 1.21 (s, 3 H), 1.73 (dd, 1 H, J = 12.7 and 7.8 Hz), 2.10 (dd, 1 H, J = 12.7 and 7.3 Hz), 2.97 (dd, 1 H, J = 12.2 and 8.3 Hz), 3.21 (dd, 1 H, J = 12.2 and 3.4 Hz), 3.5–3.7 (m, 3 H), 3.7–4.0 (m, 2 H), 7.2–7.4 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ (*two signals overlapping) 25.3 (q), 25.5 (q), 32.2 (t), 40.0 (s), 41.0 (t), 41.4 (t), 42.2 (t), 54.7 (d), 127.5 (d), 128.2 (d)*, 128.2 (s), 133.2 (d)*. Anal. Calcd for $C_{15}H_{20}NOClSe$: C, 52.26; H, 5.85; N, 4.06. Found: C, 52.32; H, 5.94; N, 4.20.

To a suspension of LAH (20 mg, 0.52 mmol) in diethyl ether (2 mL) was added a solution of aluminum chloride (23 mg, 0.17 mmol) in the same solvent (2 mL),[14] and the resulting mixture was stirred at ambient temperature for 5 min. Then a solution of **16d** (X = Cl) (90 mg, 0.26 mmol) in diethyl ether (2 mL) was added, and the resulting mixture was stirred at ambient temperature for 15 min. After the workup, column chromatography [silica gel, hexane–ethyl acetate (10:1) as eluant] afforded *N*-(2-chloroethyl)-3,3-dimethyl-5-[(phenylseleno)methyl]pyrrolidine (**17d**; X = Cl) (68 mg, 0.21 mmol, 79%): IR (film) 2950, 1480, 740, and 695 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.02 (s, 3 H), 1.12 (s, 3 H), 1.55 (dd, 1 H, J = 12.7 and 7.8 Hz), 1.80 (dd, 1 H, J = 12.7 and 7.8 Hz), 2.17 (d, 1 H, J = 8.8 Hz), 2.56 (dd, 1 H, J = 13.2 and 6.8 Hz), 2.85–2.95 (m, 1 H), 2.91 (d, 1 H, J = 8.8 Hz), 3.0–3.1 (m, 3 H), 3.48 (t, 2 H, J = 6.8 Hz), 7.2–7.3 (m, 3 H), and 7.45–7.5 (m, 2 H); ^{13}C NMR (25 MHz) δ (*two signals overlapping) 28.7 (q), 29.6 (q), 33.0 (t), 36.3 (s), 42.5 (t), 46.1 (t), 56.0 (t), 64.0 (d), 68.3 (t), 126.5 (d), 128.9 (d)*, 130.9 (s), and 132.2 (d)*; mass spectrum, M^+ 333, 331. Anal. Calcd for $C_{15}H_{22}NClSe$: C, 54.47; H, 6.70; N, 4.23. Found: C, 54.46; H, 6.62; N, 4.40.

***N*-(2-Chloropropyl)-2,2-dimethyl-4-[(phenylseleno)methyl]-γ-butyrolactam (19)**: IR (film) 1690 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.09 (s, 3 H), 1.19 (s, 3 H), 1.68 (dd, 1 H, J = 12.7 and 7.3 Hz), 1.8–1.9 (m, 1 H), 1.9–2.0 (m, 1 H), 2.13 (dd, 1 H, J = 12.7 and 7.3 Hz), 2.88 (dd, 1 H, J = 12.2 and 8.8 Hz), 3.10 (ddd, 1 H, J = 14.2, 8.3 and 5.9 Hz), 3.28 (dd, 1 H, J = 12.2 and 3.4 Hz), 3.48 (dt, 1 H, J = 11.2 and 6.3 Hz), 3.49 (dt, 1 H, J = 11.2 and 6.3 Hz), 3.58 (ddd, 1 H, J = 14.2, 8.3, and 6.2 Hz), 3.73 (ddt, 1 H, J = 8.8, 3.4, and 7.3 Hz), 7.25–7.35 (m, 3 H), and 7.5–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ 25.5 (q)*, 30.4 (t), 32.2 (t), 38.2 (t), 40.0 (s), 40.8 (t), 42.3 (t), 54.4 (d), 127.4 (d), 129.2 (d)*, 129.2 (s), 133.1 (d)*, and 180.1 (s). Anal. Calcd for $C_{16}H_{22}NOClSe$: C, 53.57; H, 6.18; N, 3.90. Found: C, 53.73; H, 6.26; N, 3.99.

***N*-(2-Chloroethyl)-2,2-dimethyl-4-(phenylseleno)-5-phenyl-δ-valerolactam (21)**: IR (film) 1640 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.31 (s, 3 H), 1.33 (s, 3 H), 2.02 (dd, 1 H, J = 14.0 and 10.3 Hz), 2.05 (dd, 1 H, J = 14.0 and 4.4 Hz), 2.81 (ddd, 1 H, J = 14.2, 7.3, and 6.8 Hz), 3.40 (ddd, 1 H, J = 11.2, 6.8, and 4.9 Hz), 3.52 (ddd, 1 H, J = 10.3, 7.8, and 4.4 Hz), 3.69 (ddd, 1 H, J = 11.2, 7.3, and 6.8 Hz), 3.95 (ddd, 1 H, J = 14.2, 6.8, and 4.9 Hz), 4.68 (d, 1 H, J = 7.8 Hz), 7.2–7.5 (m, 10 H); ^{13}C NMR (25 MHz) δ 27.4 (q), 28.7 (q), 39.1 (s), 41.0 (t), 41.4 (t), 43.3 (d), 47.6 (t), 69.2 (d), 176.1 (s), and phenyl signals. Anal. Calcd for $C_{21}H_{24}NOClSe$: C, 59.94; H, 5.75; N, 3.33. Found: C, 59.75; H, 5.84; N, 3.27.

Preparation of Methyl *N*-Butyl-2-phenylpent-4-enimidate (25). Preparation of methyl 2-phenylethanimidate hydrochloride (from benzyl cyanide, methanol, and dry hydrogen chloride) and its reaction with butylamine were carried out in reported procedures.[20] To a solution of LDA (5.2 mmol) in THF (20 mL) and hexane (3.5 mL) was added a THF (5 mL) solution of methyl *N*-butyl-2-phenylethanimidate (1.02 g, 5.0 mmol) thus prepared at −78 °C under nitrogen atmosphere, and the resulting solution was stirred at −78 °C for 0.5 h. Then allyl bromide (0.43 mL, 5.0 mmol) was added, and the solution was stirred at −78 to −40 °C for 3 h. After the workup as described above, column chromatography [aluminum oxide, Woelm B (type W 200) activity grade V, hexane as eluant] afforded **25** (0.950 g, 3.9 mmol, 78%): IR (film) 1675 cm^{-1}; ^{1}H NMR (100 MHz) δ 0.88 (t, 3 H, J = 7.1 Hz), 1.1–1.6 (m, 4 H), 2.4–2.9 (m, 2 H), 3.1–3.4 (m, 2 H), 3.64 (s, 3 H), 3.95 (dd, 1 H, J = 8.8 and 6.8 Hz), 4.99 (br d, 1 H, J = 9.8 Hz),

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5.03 (br d, 1 H, J = 17.1 Hz), 5.73 (ddt, 1 H, J = 17.1, 9.8, and 6.8 Hz), and 7.1–7.4 (m, 5 H). Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.01; H, 9.43; N, 5.65.

Reaction of 25 with Phenylselenenyl Bromide. To a solution of **25** (0.123 g, 0.5 mmol) in acetonitrile (47 mL) was added a solution of phenylselenenyl bromide (0.130 g, 0.55 mmol) in the same solvent (3 mL) at 0 °C, and the resulting solution was stirred at 0 °C for 12 h. After evaporation of solvents under reduced pressure, the residual oil was purified by column chromatography [Florisil, hexane–ethyl acetate (5:1) as eluant] to give *N*-butyl-2-phenyl-4-[(phenylseleno)methyl]-γ-butyrolactam (**26**) (0.155 g, 0.40 mmol, 80%) (a mixture of two isomers; ca. 55:45): IR (film) 1690 cm^{-1}; ^1H NMR (100 MHz) δ 0.89 (t, 3 H, J = 6.8 Hz), 1.0–1.6 (m, 4 H), 1.7–2.1 (m, 1 H), 2.2–2.5 (m, 1 H), 2.5–3.1 (m, 2 H), 3.1–3.4 (m, 1 H), 3.5–4.0 (m, 3 H), 7.1–7.4 (m, 8 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ major isomer 13.7 (q), 20.1 (t), 29.5 (t), 32.3 (t), 34.2 (t), 40.5 (t), 47.7 (d), 55.5 (d), 174.9 (s), and phenyl signals; minor isomer 13.7 (q), 20.1 (t), 29.4 (t), 31.4 (t), 34.3 (t), 40.2 (t), 46.9 (d), 55.3 (d), 174.5 (s), and phenyl signals; mass spectrum, M^+ 387, 385.

To a suspension of LAH (0.030 g, 0.8 mmol) in diethyl ether (5 mL) was added a solution of **26** (0.237 g, 0.6 mmol) in the same solvent (5 mL) at 0 °C, and the resulting mixture was stirred at ambient temperature for 2 h. After the usual workup,[4g] column chromatography [silica gel, hexane–ethyl acetate (10:1) as eluant] afforded *N*-butyl-4-phenyl-2-[(phenylseleno)methyl]pyrrolidine (**27**) (0.120 g, 0.32 mmol, 54%) (mixture of two isomers; ca. 63:37): IR (film) 2955, 2930, 1480, 740, 700, and 695 cm^{-1}; ^1H NMR (100 MHz) δ 0.91 (t, 3 H, J = 7.1 Hz), 1.1–1.6 (m, 4 H), 1.7–2.0 (m, 1 H), 2.0–2.3 (m, 1 H), 2.3–2.6 (m, 1 H), 2.6–3.0 (m, 3 H), 3.0–3.4 (m, 4 H), 7.1–7.4 (m, 8 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ major isomer 14.0 (q), 20.6 (t), 31.0 (t), 32.6 (t), 41.3 (t), 41.3 (d), 54.2 (t), 61.5 (t), 65.0 (d), and phenyl signals; minor isomers 14.0 (q), 20.7 (t), 30.9 (t), 33.9 (t), 38.8 (t), 42.1 (d), 54.5 (t), 62.1 (t), 64.1 (d), and phenyl signals; mass spectrum, M^+ 373, 371. Anal. Calcd for $C_{21}H_{27}NSe$: C, 67.73; H, 7.31; N, 3.76. Found: C, 67.70; H, 7.29; N, 3.98.

Ring Enlargement to 6,6-Dimethyl-8-[(phenylseleno)methyl]-1-oxa-4-azacyclooctane (32). *N*-(2-Chloroethyl)-2,2-dimethylpent-4-enamide (**30**) was prepared from **15d** and hydrogen chloride by the reported procedure:[15] IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 1.20 (s, 6 H), 2.21 (br d, 2 H, J = 7.3 Hz), 3.5–3.65 (m, 4 H), 4.9–5.2 (m, 2 H), 5.71 (ddt, 1 H, J = 17.6, 9.3, and 7.3 Hz), and 5.9–6.2 (br s, 1 H); high-resolution mass spectrum, calcd for $C_9H_{16}NOCl$ 189.0920, 191.0891; found 189.0932, 191.0913.

To a solution of **30** (0.150 g, 0.78 mmol) in acetonitrile (5 mL) was added a solution of phenylselenenyl bromide (0.187 g, 0.79 mmol) in the same solvent (3 mL), and the resulting solution was stirred at ambient temperature for 2 h. After the workup as described above, column chromatography [aluminum oxide, Woelm B (type W 200) activity grade V, hexane–ethyl acetate (10:1) as eluant] afforded *N*-(2-chloroethyl)-2,2-dimethyl-4-[(phenylseleno)methyl]imino-γ-butyrolactone (**31**) (0.220 g, 0.64 mmol, 81%): IR (film) 1707 cm^{-1}; ^1H NMR (100 MHz) δ 1.19 (s, 3 H), 1.24 (s, 3 H), 1.71 (dd, 1 H, J = 12.7 and 9.8 Hz), 2.12 (dd, 1 H, J = 12.2 and 5.9 Hz), 3.07 (dd, 1 H, J = 12.7 and 6.8 Hz), 3.17 (dd, 1 H, J = 12.7 and 5.9 Hz), 3.35–3.7 (m, 4 H), 4.4–4.7 (m, 1 H), 7.2–7.3 (m, 3 H), and 7.45–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ 26.2 (q), 26.4 (q), 32.2 (t), 40.8 (s), 44.3 (t), 44.6 (t), 48.8 (t), 77.6 (d), 127.2 (d), 129.1 (d)*, 129.4 (s), 132.9 (d)*, and 169.3 (s); mass spectrum, M^+ 347, 345. Anal. Calcd for $C_{15}H_{20}NOClSe$: C, 52.26; H, 5.85; N, 4.06. Found: C, 52.21; H, 5.66; N, 3.75.

To the suspension of LAH (0.041 g, 1.08 mmol) in diethyl ether (2 mL) was added a solution of **31** (0.124 g, 0.36 mmol) in the same solvent (1 mL) at 0 °C, and the resulting mixture was stirred at ambient temperature for 1.5 h. After the usual workup, column chromatography [silica gel, hexane–ethyl acetate (1:1) as eluant] afforded **32** (0.100 g, 0.32 mmol, 89%): IR (film) 3150, 3070, 2960, 1480, 1020, 740, and 695 cm^{-1}; ^1H NMR (400 MHz) δ 0.88 (s, 3 H), 1.03 (s, 3 H), 1.19 (dd, 1 H, J = 6.8 and 3.9 Hz), 1.21 (dd, 1 H, J = 6.8 and 3.9 Hz), 1.55 (d, 1 H, J = 12.2 Hz), 1.6–1.7 (m, 2 H), 1.79 (dd, 1 H, J = 5.9 and 3.9 Hz), 1.90 (dd, 1 H, J = 5.9 and 3.9 Hz), 2.73 (d, 1 H, J = 11.7 Hz), 2.94 (dd, 1 H, J = 11.7 and 5.9 Hz), 3.14 (dd, 1 H, J = 11.7 and 6.8 Hz), 3.9–4.1 (m, 1 H), 7.2–7.3 (m, 3 H), 7.5–7.55 (m, 2 H), and 7.85–7.95 (br s, 1 H); ^{13}C NMR (25 MHz) δ 24.0 (q, CH_3), 25.4 (t, C_7), 29.4 (t, $SeCH_2$), 30.7 (q, CH_3), 35.7 (s, C_6), 36.7 (t, CH_2N), 50.4 (t, CH_2N), 67.0 (d, CHO), 71.5 (t, CH_2O), 126.4 (d), 128.8 (d)*, 131.2 (s), and 132.2 (d)*; mass spectrum, M^+ 313, 311. Anal. Calcd for $C_{15}H_{23}NOSe$: C, 57.69; H, 7.42; N, 4.48. Found: C, 57.62; H, 7.34; N, 4.46.

7,7-Dimethyl-9-[(phenylseleno)methyl]-1-oxa-5-azacyclononane (35): IR (film) 3070, 3030, 2960, 2930, 2840, 1470, 1440, 735, and 690 cm^{-1}; ^1H NMR (100 MHz) δ 0.85 (s, 3 H), 0.88 (s, 3 H), 1.46 (dd, 1 H, J = 14.7 and 9.3 Hz), 1.56 (dd, 1 H, J = 14.7 and 2.4 Hz), 2.06 (quint, 2 H, J = 7.3 Hz), 2.31 (s, 2 H), 2.3–2.7 (m, 1 H), 2.96 (dd, 1 H, J = 11.7 and 6.4 Hz), 3.09 (dd, 1 H, J = 11.7 and 6.4 Hz), 3.2–3.4 (m, 3 H), 3.92 (ddt, 1 H, J = 9.3, 2.4, and 6.4 Hz), 7.1–7.3 (m, 3 H), 7.4–7.6 (m, 2 H), and 8.6–9.2 (br s, 1 H); ^{13}C NMR (25 MHz) δ 17.7 (t, C_8), 23.6 (q, CH_3), 31.1 (q, CH_3), 35.2 (s, C_7), 36.5 (t, $SeCH_2$), 50.1 (t, C_3), 56.7 (t, CH_2N)*, 66.9 (d, CHO), 70.8 (t, CH_2O), 127.2 (d), 128.8 (d)*, 131.2 (s), and 132.0 (d)*; mass spectrum, M^+ 327, 325. Anal. Calcd for $C_{16}H_{25}NOSe$: C, 58.89; H, 7.72; N, 4.29. Found: C, 58.51; H, 7.76; N, 4.22.

Cyclization to 2,2-Dimethyl-5-[(phenylseleno)methyl]-δ-valerolactone (37). *N*-(2-Chloroethyl)-2,2-dimethylhex-5-enamide (**36**) was prepared from **23** and hydrogen chloride by a reported procedure:[15] IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 1.20 (s, 6 H), 1.45–1.75 (m, 2 H), 1.85–2.1 (m, 2 H), 3.50–3.65 (m, 4 H), 4.94 (br d, 1 H, J = 9.8 Hz), 4.99 (br d, 1 H, J = 17.1 Hz), 5.80 (ddt, 1 H, J = 17.1, 9.8, and 6.4 Hz), and 6.0–6.1 (br s, 1 H); high-resolution mass spectrum, M^+ calcd for $C_{10}H_{18}NOCl$ 203.1077, 205.1047; found 203.1057, 205.1048.

To a solution of **36** (0.408 g, 2.0 mmol) in acetonitrile (10 mL) was added a solution of phenylselenenyl bromide (0.471 g, 2.0 mmol) in the same solvent (10 mL), and the resulting solution was stirred at ambient temperature for 12 h. After the workup as described above, column chromatography [silica gel, hexane–ethyl acetate (5:1) as eluant] afforded **37** (0.281 g, 0.95 mmol, 47%): IR (film) 1725 cm^{-1}; ^1H NMR (100 MHz) δ 1.28 (s, 6 H), 1.6–1.8 (m, 2 H), 1.8–2.2 (m, 2 H), 3.08 (dd, 1 H, J = 12.7 and 7.8 Hz), 3.20 (dd, 1 H, J = 12.7 and 4.4 Hz), 4.3–4.6 (m, 1 H), 7.2–7.3 (m, 3 H), and 7.4–7.6 (m, 2 H); ^{13}C NMR (25 MHz) δ 25.2 (t), 27.4 (q), 27.5 (q), 32.6 (t), 33.8 (t), 37.7 (s), 80.2 (d), 127.1 (d), 129.1 (d)*, 129.6 (s), 132.4 (d)*, and 176.3 (s). Anal. Calcd for $C_{14}H_{18}O_2Se$: C, 56.57; H, 6.10. Found: C, 56.93; H, 6.14.

Oxidative Elimination of 21 to *N*-(2-Chloroethyl)-3,3-dimethyl-6-phenyl-1-azacyclohex-5-en-2-one (38). Ozonization of **21** (0.273 g, 0.65 mmol) was carried out in dichloromethane (10 mL) at −78 °C. The cold solution was then added to refluxing carbon tetrachloride (25 mL) containing triethylamine (10 mmol) as reported in the literature.[21] After evaporation of solvents, column chromatography [silica gel, hexane–ethyl acetate (10:1) as eluant] afforded **38** (0.150 g, 0.57 mmol, 88%): IR (film) 1670 cm^{-1}; ^1H NMR (100 MHz) δ 1.23 (s, 6 H), 2.26 (d, 2 H, J = 5.1 Hz), 3.45 (t, 1 H, J = 6.5 Hz), 3.46 (t, 1 H, J = 6.5 Hz), 3.81 (t, 1 H, J = 6.5 Hz), 3.82 (t, 1 H, J = 6.5 Hz), 5.28 (t, 1 H, J = 5.1 Hz), and 7.2–7.4 (m, 5 H); ^{13}C NMR (25 MHz) δ 24.5 (q)*, 34.8 (t), 37.4 (s), 41.6 (t), 44.8 (t), 108.9 (d), 127.5 (d)*, 128.4 (d), 128.6 (d)*, 136.0 (s), 141.1 (s), and 176.8 (s); high-resolution mass spectrum, M^+ calcd for $C_{15}H_{18}NOCl$ 263.1077, 265.1047; found 263.1088, 265.1029.

Reductive Removal of Phenylseleno Group from 21 to *N*-(2-Chloroethyl)-2,2-dimethyl-5-phenyl-δ-valerolactam (39). To a solution of nickel(II) chloride hexahydrate (0.998 g, 4.2 mmol) in methyl alcohol (4 mL) was added a solution of **21** (0.575 g, 1.4 mmol) in THF (16 mL) at ambient temperature. Then the solution was cooled in an ice bath, and sodium borohydride (0.476 g, 12.6 mmol) was added in small portions. After stirring at 0 °C for 20 min, a black precipitate thus formed was filtered over Celite, and the filtrate was evaporated to leave a pale yellow oil which was purified by preparative TLC [Merck, silica gel 60 F_{254} PLC plate (20 cm × 20 cm × 2 mm), hexane–ethyl acetate (2:1) as eluant] to give **39** (0.210 g, 0.45 mmol, 32%): IR (film) 1640 cm^{-1}; ^1H NMR (100 MHz) δ 1.29 (s, 6 H), 1.2–1.6 (m, 1 H), 1.6–2.0 (m, 1 H), 2.1–2.5 (m, 1 H), 2.75 (ddd, 1 H, J = 13.7, 8.3, and 5.9 Hz), 3.3–4.0 (m, 3 H), 4.0–4.3 (m, 1 H), 4.82 (dd, 1 H, J = 4.9 and 4.4 Hz), and 7.0–7.7 (m, 5 H); ^{13}C NMR (25 MHz) δ 27.5 (q), 28.0

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(q), 28.0 (t), 31.4 (t), 38.3 (s), 41.6 (t), 48.6 (t), 63.6 (d), 177.3 (s), and phenyl signals; high-resolution mass spectrum, M^+ calcd for $C_{15}H_{20}NOCl$ 265.1233, 267.1204; found 265.1230, 267.1208.

Supplementary Material Available: A listing of properties and full spectral data of compounds **1b–e, 2b–e, 3b, 3d,e, 5, 10–13, 15a–c, 16a–c, 16d** (X = Br, I), **17a, 17c, 17d** (X = Br), **20, 22–24, 33,** and **34** and the preparation of the authentic sample of **27** (11 pages). Ordering information is given on any current masthead page.

Unusual Reactions between 1,4-Dihydropyridines and 1,2,4,5-Tetrazines in the Presence of K-10/Fe(III) Clay Catalyst

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Diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylates **1a–c** add to 3,6-dipyridyl-1,2,4,5-tetrazines **2a–c** according to two different routes, neither of which is the anticipated inverse electron demand Diels–Alder reaction with **1** as dienophile and **2** as diene. The first route is followed by NH compounds **1a–c**; they undergo a "hydrogen-transfer" reaction which can be catalyzed by K-10/Fe(III) clay. *N*-Methyl-1,4-dihydropyridine **1d** undergoes a different dehydrogenation, leading to 2-methylene-1,2-dihydropyridine derivative **7**, which, in turn, adds to **2** with nitrogen loss, leading to a spiro bicyclic intermediate **8**, whose aromatization gives the open-chain pyridazines **5a–c**. These are easily converted into their cyclized counterpart (**6a–c**) with the attendant loss of ethanol.

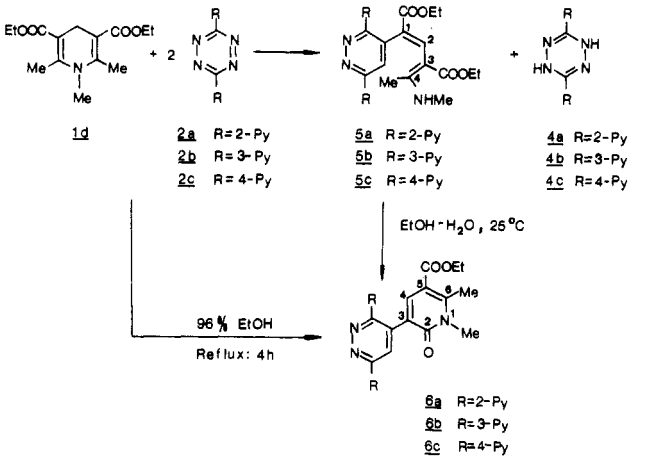
Catalysis of organic reactions by inorganic solids often allows one to run reactions at ambient temperature and pressure, with high yields and selectivities.[1] We have shown that 1,4-dihydropyridines can be aromatized efficiently in the presence of clay catalysts.[2] Some heterocyclic systems, when submitted to the nitrating reagent "clayfen",[3] give rise to quite interesting products.[4] We report here somewhat unexpected reaction pathways, some of which are catalyzed by the modified K-10 montmorillonite exchanged with ferric ions.

Our initial plan was to perform a Diels–Alder reaction, since diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (**1a**) can serve as a dienophile in a [4 + 2] cycloaddition involving a hetero diene as the reaction partner.[5] For this latter role, we chose 1,2,4,5-tetrazines, which are known to be excellent dienes in inverse electron demand Diels–Alder reactions.[6] They have been shown to participate in Diels–Alder reactions with a number of olefinic and acetylenic dienophiles to produce 1,4-dihydropyridazines, 4,5-dihydropyridazines, and pyridazines.[6] Only a limited group of nitrogen-containing heterocyclic compounds, such as 1-methylpyrrole,[7] 1-methylimidazole, and indole[8] have been used as dienophiles in such cycloadditions.

We report here our first results on the reactions of diethyl 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylates **1a–d**[9-12] with 3,6-dipyridyl-1,2,4,5-tetrazines **2a–c**.[13,14] A first unexpected finding was that compounds **1a–c** (R^2 = H), instead of the anticipated Diels–Alder reaction, undergo a "hydrogen-transfer" reaction converting them into the corresponding pyridines (**3a–c**), the tetrazine **2** serving as the acceptor of an hydrogen molecule (details in the supplementary material).

This facile oxidation route is subject to catalysis by the acidic K-10 montmorillonite doped with ferric ions according to the standard procedure.[15] We had already reported its use for catalysis of Diels–Alder reactions.[16,17] Here this catalyst appears to speed up the reaction of the

Scheme I



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